

Mating Scheme For Production Of HbA Replacement Mice

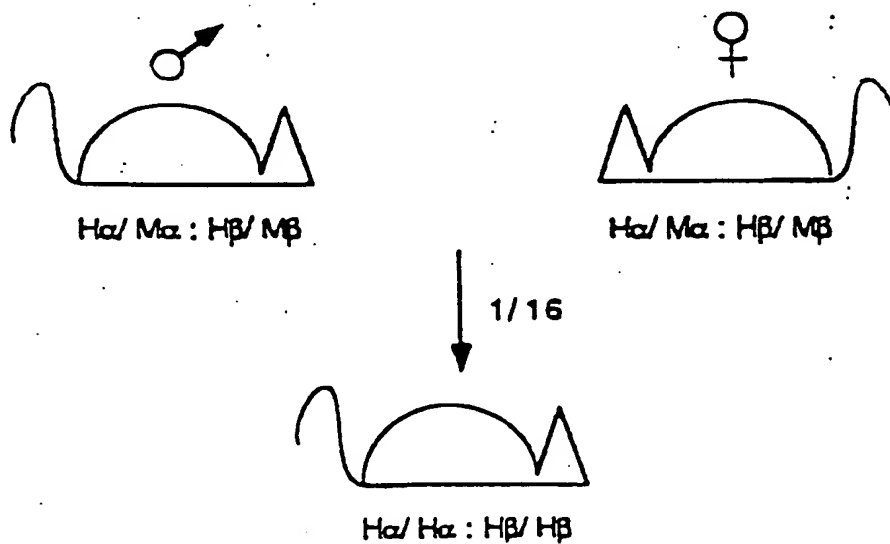
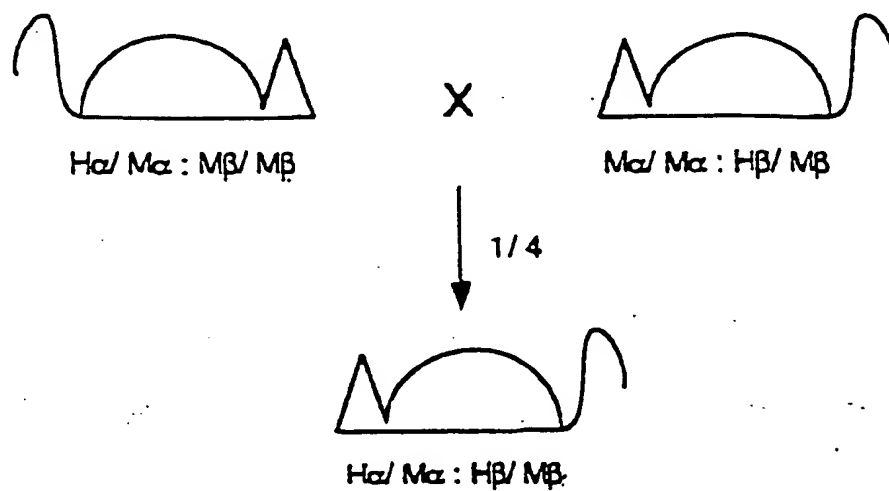
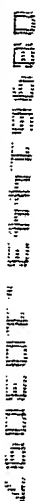


FIG. 1

Mouse β ko/human β replacement



Human Replacement Of The Mouse β -Globin Locus

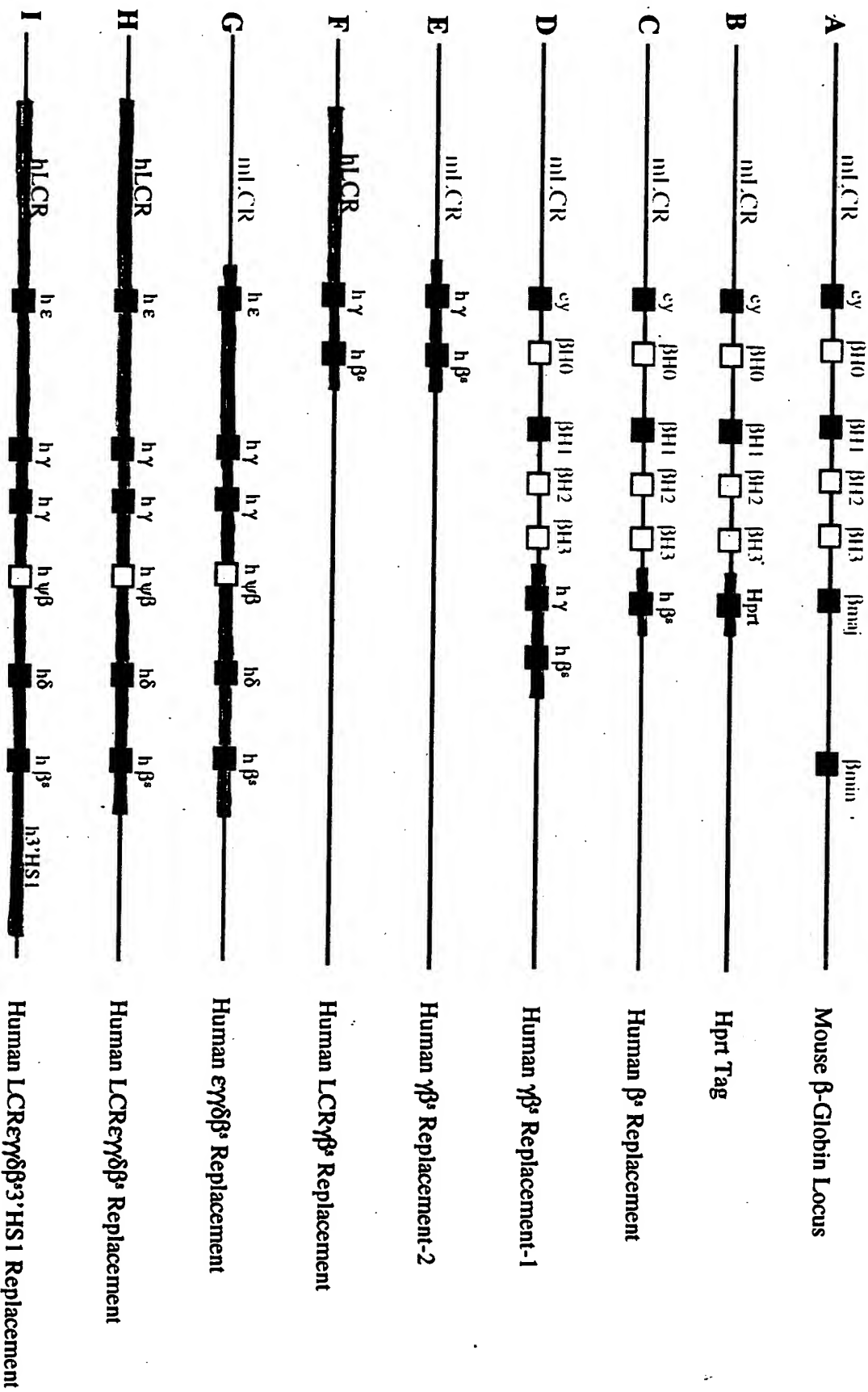


Fig. 3

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A mLCR m ζ m α 1 m α 2
Mouse α -Globin Locus

B mLCR m ζ Hprt
Hprt Tag

C mLCR m ζ h α 1
Human α 1 Replacement

D mLCR m ζ h α 2 h α 1
Human α 2 α 1 Replacement

E mLCR h ζ 2 $\psi\zeta$ 1 $\psi\alpha$ 2 $\psi\alpha$ 1 h α 2 h α 1
Human ζ 2 α 2 α 1 Replacement

F mLCR h α 1
Human α 1 Replacement

G mLCR h α 2 h α 1
Human α 2 α 1 Replacement

[illegible]

Production Of Transgenic HbF \rightarrow HbA Mice
(Doubly Homozygous For Mouse α -Globin And β -Globin Deletions)

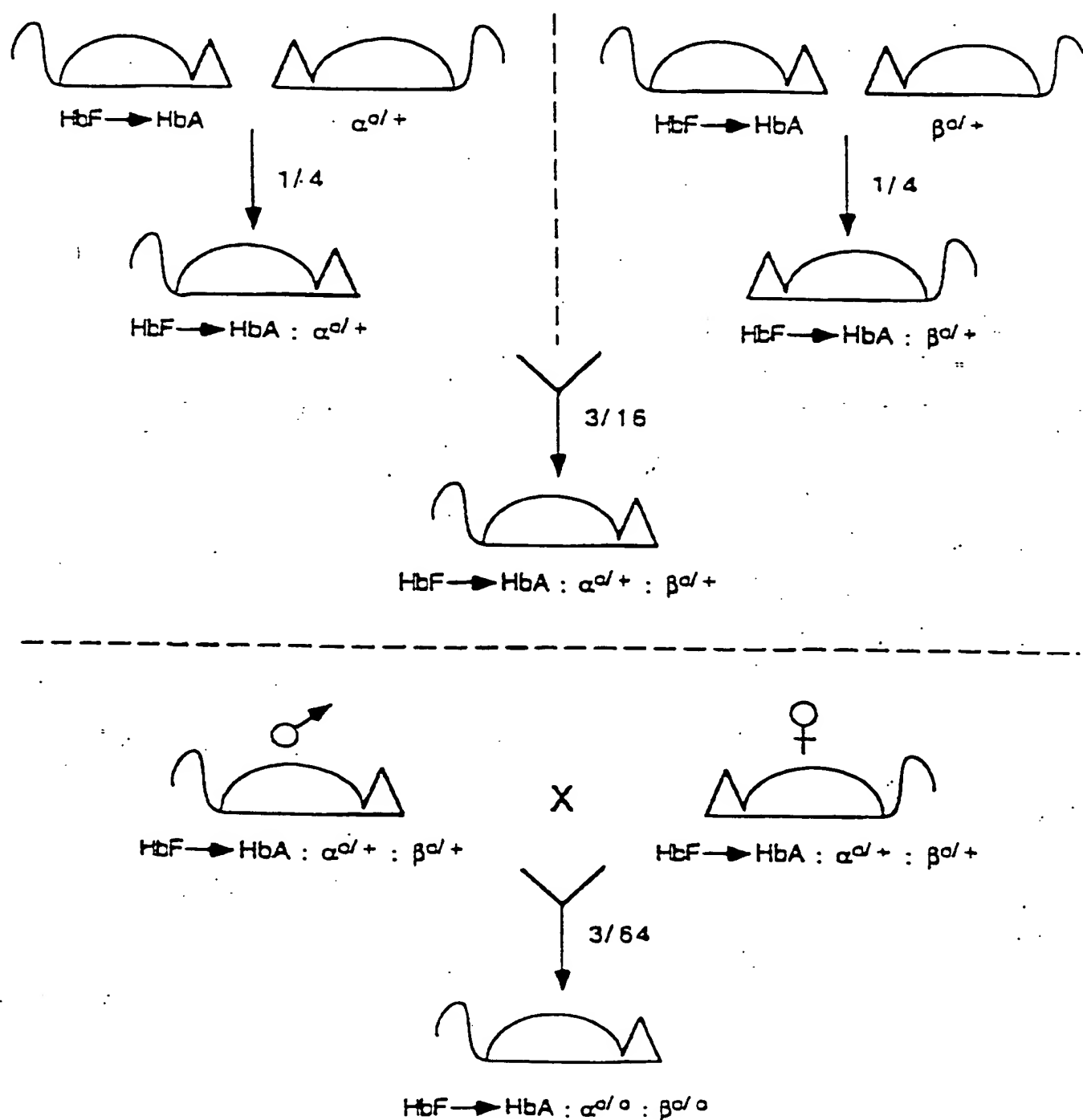
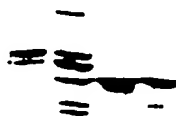


FIG. 5

Isoelectric Focusing Gel Of Transgenic Mouse Hemolysates

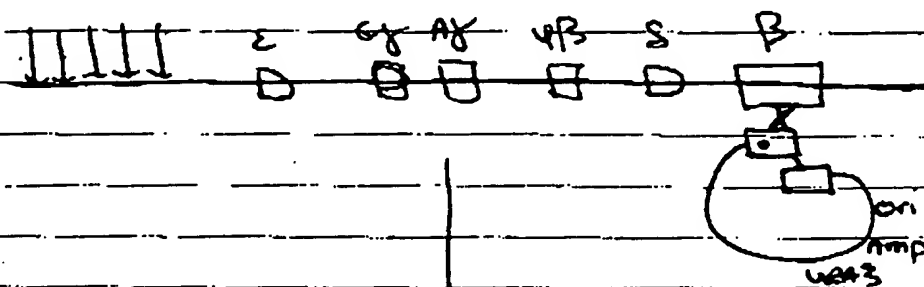
1 2 3 4



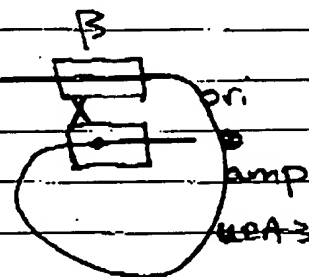
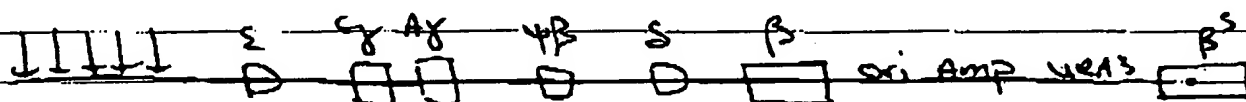
1. Mouse Control
2. HbF \rightarrow HbA : $\alpha^{+/+}$: $\beta^{+/+}$ Mouse
3. HbF \rightarrow HbA : $\alpha^{o/o}$: $\beta^{o/o}$ Mouse
4. Human AA Control

FIG. 6

YAC



select for URA3⁺



select for URA3⁻
(5-fluoro-orotic acid)

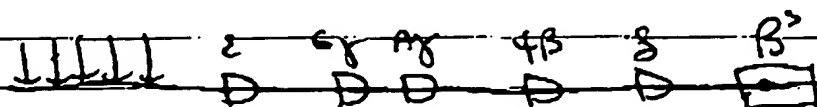
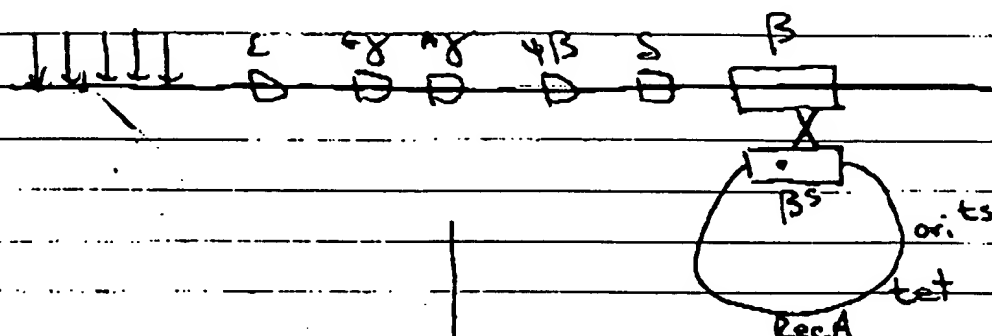
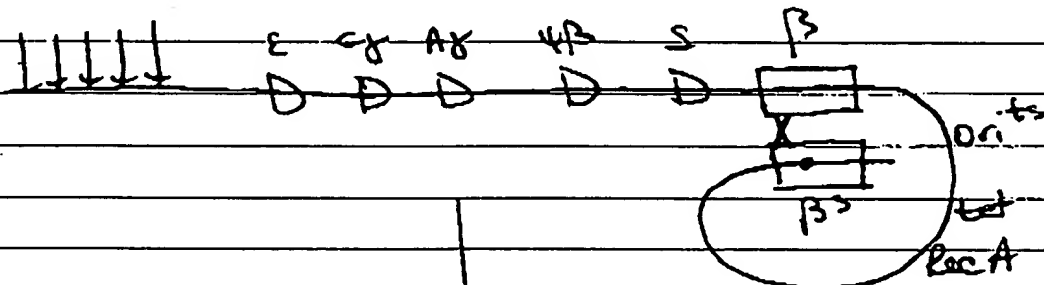
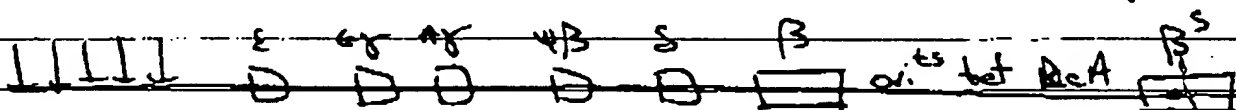


FIG. 8

BAC



select for tet^R at 43°C
(non-permissive temp for ori^{ts})



select for tet^S (Fusaric Acid)
at 37°C

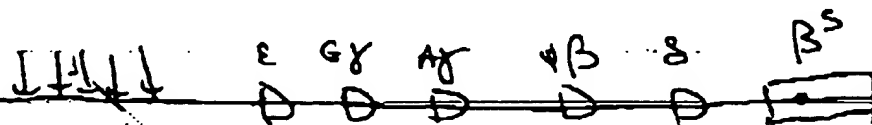


FIG. 9A

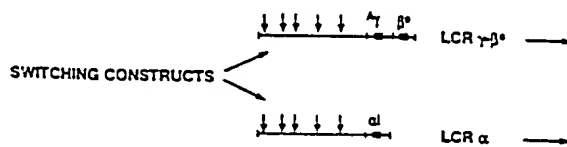
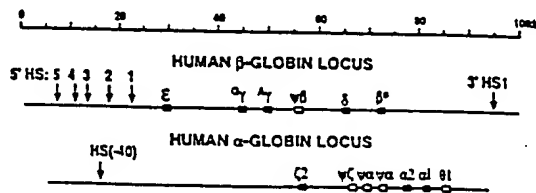


FIG. 9C

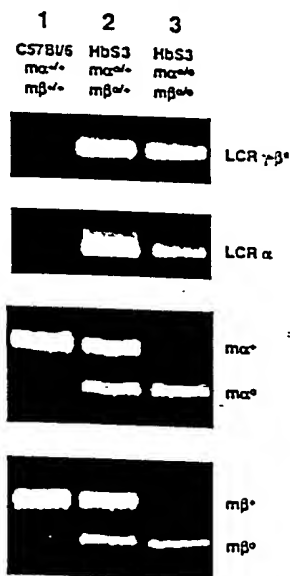
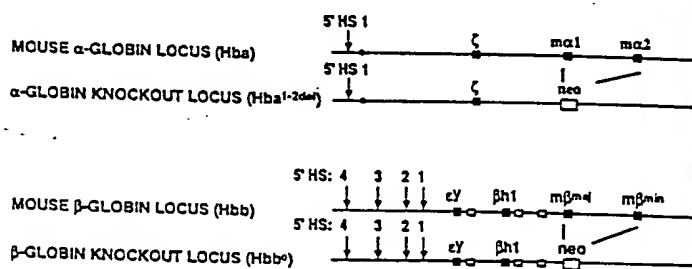


FIG. 9B



This gel electrophoresis image displays the separation of hemoglobin S (HbS) and hemoglobin F (HbF) in various samples. The lanes are labeled at the top: 'Mouse Negative Control', 'HbS2', 'HbS3', 'HbS4', 'HbS5', and 'Man HbSS Control'. On the left side, the bands are identified as 'mHbA' (mouse hemoglobin A) and 'HbF' (human hemoglobin F). On the right side, the bands are identified as 'HbS' (human hemoglobin S) and 'HbF' (human hemoglobin F). The 'Mouse Negative Control' lane shows a single band at the mHbA position. The 'HbS2', 'HbS3', 'HbS4', and 'HbS5' lanes show a single band at the HbS position. The 'Man HbSS Control' lane shows a single band at the HbS position. The 'HbF' bands are visible in the 'HbS2', 'HbS3', 'HbS4', and 'HbS5' lanes, indicating the presence of HbF in these samples.

FIG. 10

FIG. 11A

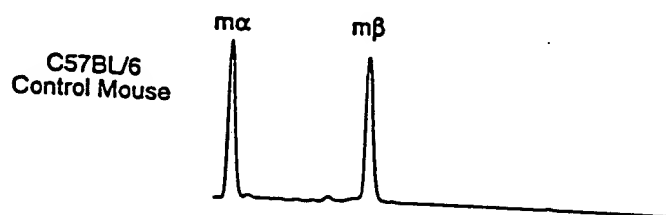


FIG. 11B

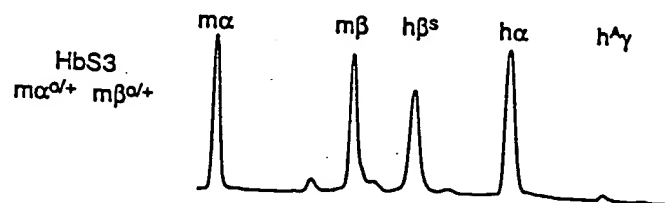


FIG. 11C

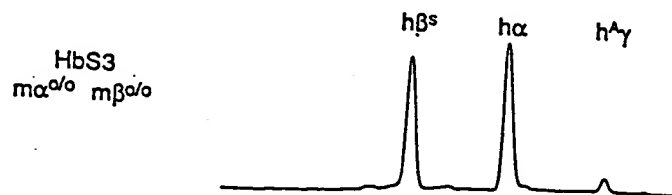
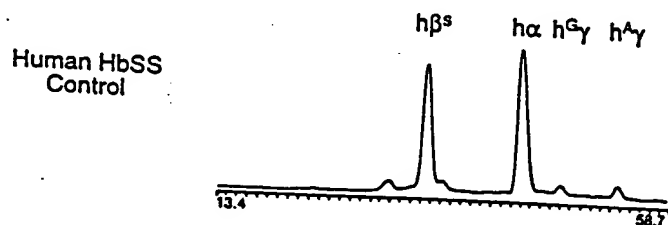


FIG. 11D



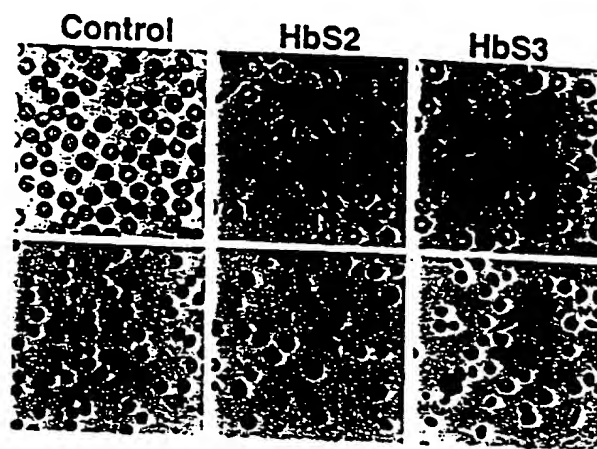


FIG. 12

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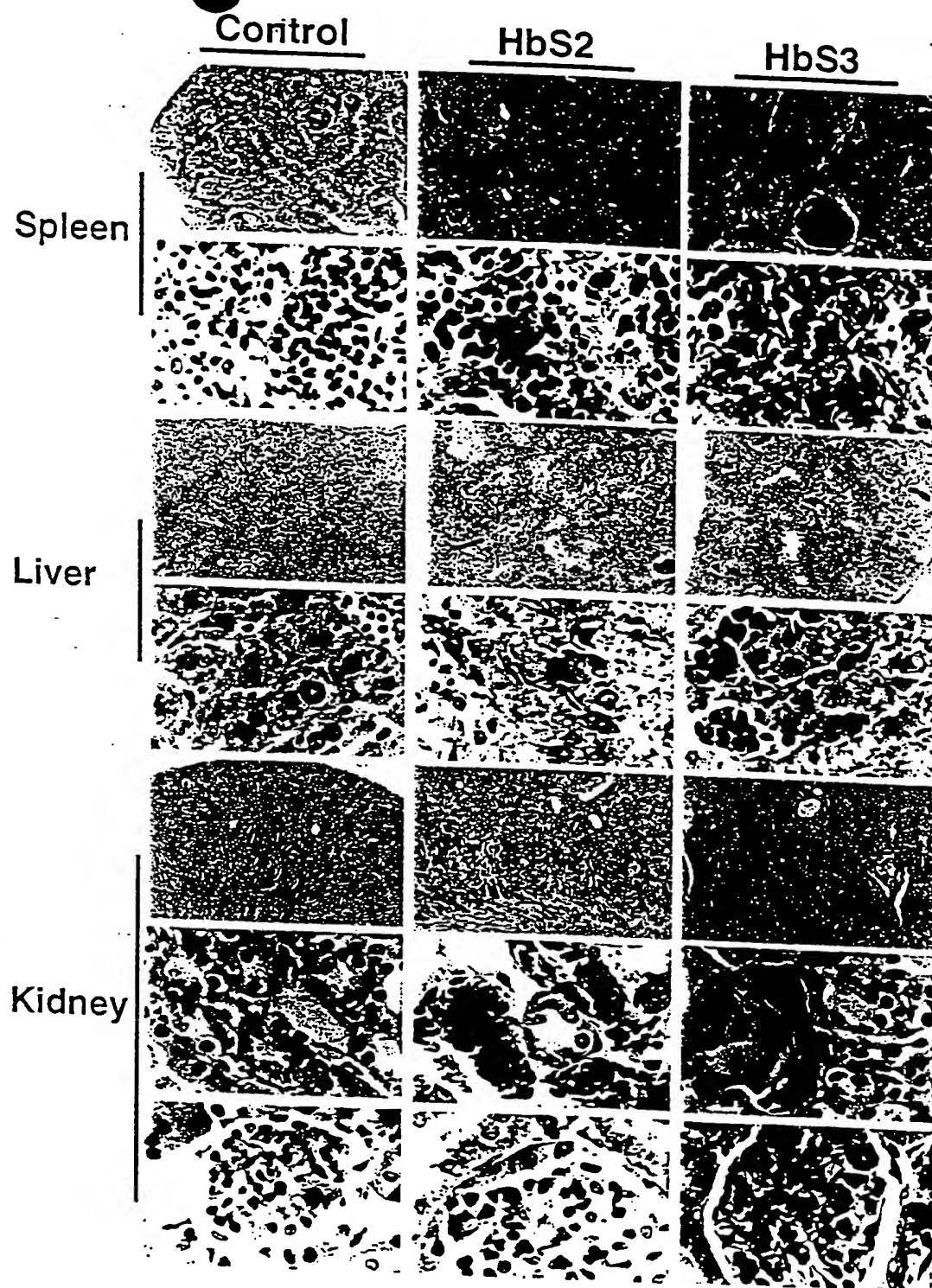


FIG. 13

FIG. 14A



FIG. 14B



Hemoglobin Switching In HbA Mice

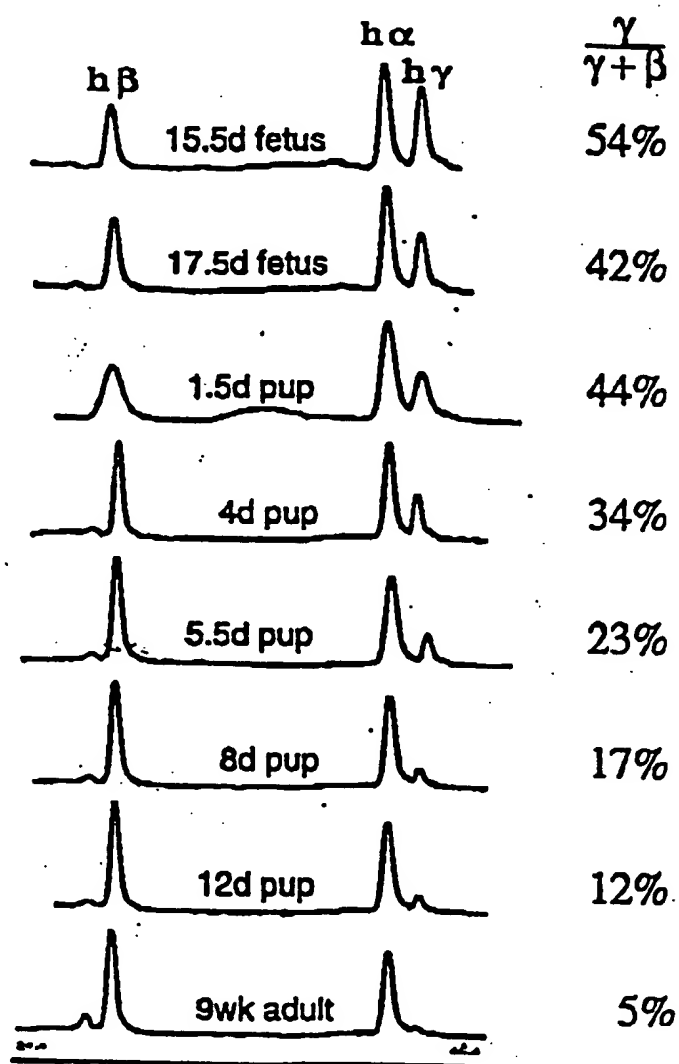


FIG. 15

**Increasing HbF Levels In HbS Mice:
Crossing The HbS 3 and HbF Lines**

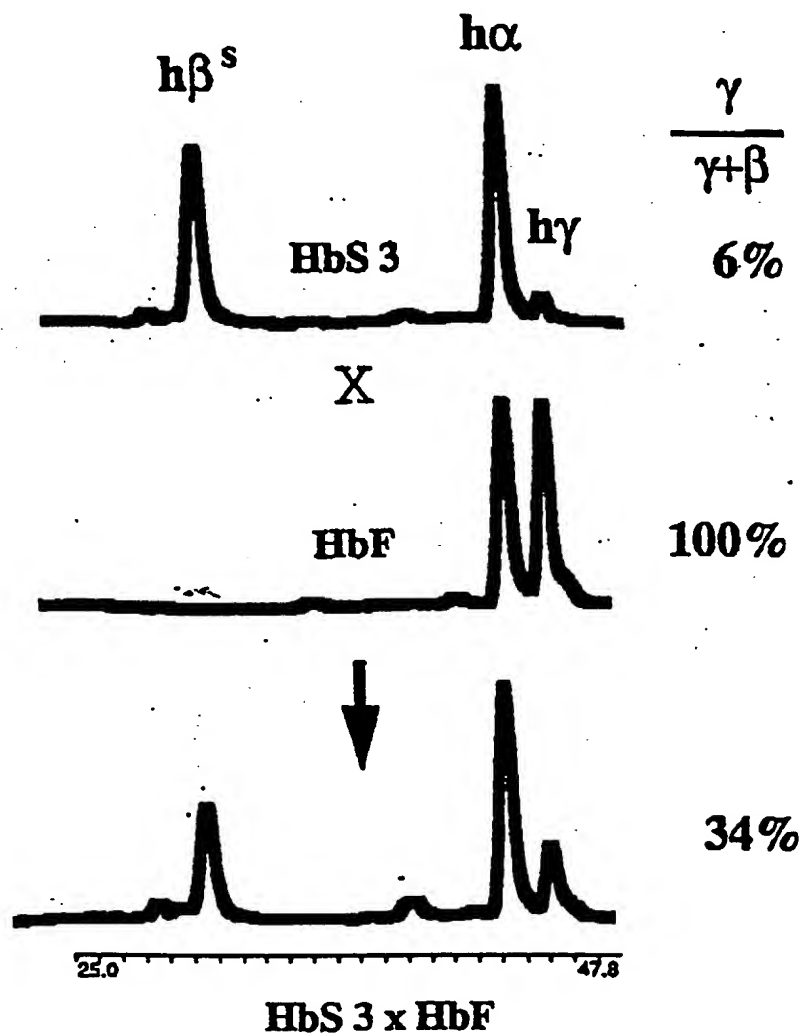


FIG. 16